REMARKS

Applicants have added claims 22 and 23 which depend on claim 8. Support for these claims is found e.g., on page 2, line 9 to page 4, last line.

Claims 1 and 6 stand rejected under 35 U.S.C. § 103(a) for purportedly being unpatenable over Dowson and Kell already of record. Applicants disagree.

Applicants claim a general method for testing *S. pnuemoniae* for penicillin resistance by isolating DNA from *S. pnuemoniae* having an unknown resistance to penicillin and then hybridizing that DNA to a probe that specifically hybridizes to PBP gene from a penicillin sensitive strain of *S.pnuemoniae,* and a DNA probe that specifically hybridizes to a PBP gene from a penicillin resistant strain of *S.pnuemoniae* wherein the PBP gene is a PBP2x, PBP1a, or PBP2b. Neither Dowson nor Kell teach or suggest Applicant's claimed method.

Regarding Dowson, the Examiner contends that this reference teaches a method for identifying penicillin-sensitive or penicillin-resistance in streptococci previously previously not known to have antibiotic resistance (Office Action sentence spanning page 2-3). Further, the Examiner contends that Dowson provides sufficient evidence for one of skill in the art to screen any streptococci strain including *S. pneumonia.* Applicants do not agree with this assessment of the Dowson reference.

Dowson shows in Table 1 (page 5859) a number of "penicillin-sensitive and penicillin-resistant streptococci"; i.e. strains for which sensitivity or resistance to penicillin was known. Of some of the strains, the penicillin susceptibility is shown by the MIC values (see 4th column of Table 1). Clearly the designation "ND, not determined" in the 4th column of Table 1 means only that the MIC value was not measured, but this does not indicate that the bacteria's sensitivity or resistance to penicillin was unknown. Dowson as a whole does not teach or suggest determining whether the strains listed in Table 1 were sensitive or resistant to penicillin using the method and oligonucleotides described in Dowson.

Dowson may teach one sensitivity-specific probe and at least one resistant-specific probe on page 5859, right col., second full paragraph, but in every case, the probes were hybridized to streptococci where the penicillin resistance of the streptococci was already known, see page 5859, right col., third full paragraph which discusses how Dowson's probes were used :

> "None of the oligonucleotide probes hybridized to the penicillin-sensitive strains of *S. sanguis* and *S. oralis.* The 1.5kb probe from the penicillin-sensitive pneumococcus also failed to hybridize to penicillin-sensitive *S. sanguis* strains and only bound very weakly to sensitive strains of *S. oralis.* .... However, Pn13(the probe for the pneumococcal class B PBP2DR gene) and the 1.5kb probe from the penicillin-sensitive pneumococcus, hybridized strongly to each of the penicillin-resistant strains of *S. sanguis* and *S. oralis.*" (emphasis added)(page 5859, third full paragraph)

Thus Dowson does not teach or suggest a method for determining if a streptococci is penicillin resistant, because the penicillin resistance of all of Dowson's tested streptococci was known already.

Moreover, what Dowson describes is an examination of the genetic relatedness among known resistant strains of streptococci of different species. Dowson describes searching for particular classes (A and B) of *S. pneumoniae* resistant genes in other species resistant to penicillin, S. *sanguis* or *S. oralis,* by using oligonucleotide probes that are either specific for the gene of class A or specific for the gene of class B (page 5859, 2nd col., 1st full paragraph:"*Detection of Mosaic PBP2B Genes from S. pneumonia in Penicillin-Resistant S sanguis and S. oralis by Oligonucleotide Probes*").

Dowson does not teach or suggest determining whether or not a streptococci strain is sensitive to penicillin. Dowson does not teach or suggest that one of skill in the art can take any streptococci strain having unknown susceptibility to penicillin and then determine whether or not that strain is sensitive or resistant to penicillin by hybridizing its DNA with at least one sensitivity-specific probe and at least one resistance-specific probe. Dowson only

teaches and suggests hybridizing the probes to the DNA of strains or species that are already known to be sensitive or resistance to penicillin.

Thus Dowson teaches that the relatedness among various resistant streptococci species, e.g. *S. pnuemoniae, S. sanguis and S. oralis,* can be studied if probes specific to a particular class of resistance genes are used to search for a gene of that class in the genome of strains or species already known to be resistant to penicillin.

Even if Dowson teaches hybridizing sensitive-specific probes and resistant-specific probes to the DNA of various streptococci strains having known penicillin sensitivity or resistance, such disclosure does not teach or suggest a method for identifying an unknown *Streptococci pnuemoniae* as a penicillin sensitive or resistant strain, because the teaching of Dowson is limited to strains in which the sensitivity or resistance to penicillin was already known before the screening with the oligonucleotides.

Because Dowson does not teach or suggest a method for testing streptococci in general for resistance to penicillin, Dowson does not provide any incentive for testing *S. pneumonia* in particular for resistance to penicillin.

Similarly, Kell also refers to a method for studying the relatedness among resistant strains. Kell reports that little information on the relationships among resistant strains is known, and teaches one of skill in the art to choose penicillin-resistant pneumococci for gene fingerprinting to classify the penicillin-resistant pneumococci into different groups. Kell does not teach or suggest fingerprinting any pneumococci wherein the sensitivity or resistance to penicillin was not known. Therefore, Kell does not overcome the deficiencies of Dowson.

The combined teachings of Dowson and Kell do not provide any incentive to screen a pneumococci sample wherein the pneumococci's sensitivity or resistance to penicillin is not known, because both methods of Dowson and Kell are limited to samples for which the sensitivity or resistance to penicillin was already known. Both teach one of skill in the art to study the relatedness among

already known resistant strains to better understand the epidemiology of penicillin resistant streptococci. Because both references teach one of skill in the art to screen strains in which the sensitivity or resistance to penicillin was known before the screening, the combined teachings of Dowson and Kell do not provide any incentive to assay a pneumococci sample for resistance by hybridizing the DNA of the sample with at least one sensitive-specific probe and at least one resistant-specific probe. Without any indication in Dowson that they determined the penicillin sensitivity or resistance of a strain having unknown resistance using their disclosed method, one of skill in the art would not have been motivated with a reasonable expectation of success to make the claimed method. Thus, neither Dowson nor Kell alone or in combination teach or suggest Applicant's rapid general method for testing a *S. pneumoniae* for resistance to penicillin by isolating DNA from a *S. pneumoniae* of unknown resistance and contacting that DNA with a probe that is specific to a PBP of a penicillin sensitive *S. pneumoniae* and a probe that is specific to a PCP of a penicillin resistant *S. pneumoniae.* Therefore Dowson and Kell in combination fail to render the invention as claimed obvious.

In view of the foregoing remarks, Applicants request that the Examiner reconsider and withdraw the rejection of claims 1 and 6 under 35 U.S.C. 103(a) in view of Dowson and Kell.

Claims 2-3, 11, 12, 14, 19 and 21 stand rejected under 35 U.S.C. 103 for purportedly being unpatentable over Dowson in view of Kell and in further view of *In Re Deuel.*

As discussed above, Dowson in combination with Kell do not teach a general method for detecting penicillin resistance.

Dowson and Kell teach one of skill in the art to study epidemiological relatedness among penicillin resistant strains. Thus, they teach probes that are specific for particular classes of resistance genes. Therefore the probes of Dowson and Kell hybridize only to a resistance gene if the sequence of that specific class

of gene is present in the probe. The teachings of Dowson and Kell do not provide any incentive for one of skill in the art to make probes that can hybridize to various gene types of resistance, because such probes would not be specific for a particular class of resistance gene. The relatedness among different resistant strains and species as taught by Dowson and Kell could not be examined with such probes and would therefore be unsatisfactory for the intended purpose of Dowson's and Kell's methods. The MPEP, section 2143.01(V) expressly states that a proposed modification of a prior art invention cannot render that invention "unsatisfactory for its intended purpose." If it does, "there is no suggestion or motivation to make the proposed modification."

In contrast to Dowson and Kell, the particular probes used in the claimed methods have been designed to cover various types of resistance genes. The sequences of the probes recited in the claims have been optimized to obtain a clear test result independent from the class of resistance gene. As such, the combined teachings of Dowson and Kell do not teach or suggest the methods recited in claims 2-3, 11, 12, 14, 19 and 21. Therefore Dowson and Kell do not render the claimed invention obvious.

The Examiner states that Kell teaches a PBP2x gene sequence which confers antibiotic resistance wherein the sequence comprises the sequence of SEQ ID NO: 8 (Office Action page 5). However, SEQ ID NO: 8 is not related to penicillin resistance. SEQ ID NO: 8 corresponds to nucleotides 2011-2029 in line "a" of Kell's Fig. 4 (page 4387), which is a sequence of the penicillin-susceptible strain R6. Thus, SEQ ID NO: 8 does not confer any antibiotic resistance. As SEQ ID NO: 8 is not derived from penicillin-resistant pneumococci, such sequence would not suggest its use as a probe in a method to test *S.pnuemoniae* for resistance to penicillin.

In view of the foregoing remarks, Applicants request that the Examiner reconsider and withdraw the rejection of claims 2-3, 11, 12, 14, 19 and 21 under 35 U.S.C. §103 for purportedly being unpatentable over Dowson in view of Kell and in further view of *In Re Deuel*.

Claims 1-6, 8-12, 14 and 19-21 stand rejected upon the ground of nonstatutory obviousness-type double patenting for purportedly being unpatentable over claims 1-12 of US Patent no. 6,713,254. Although Applicants respectfully disagree, Applicant submit concurrently herewith a terminal disclaimer.

In view of the foregoing remarks, Applicants request that the Examiner withdraw the rejection of the claims upon the ground of nonstatutory obviousness-type double patenting for purportedly being unpatentable over claims 1-12 of US Patent no. 6,713,254.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #99380.B270037).

Respectfully submitted,

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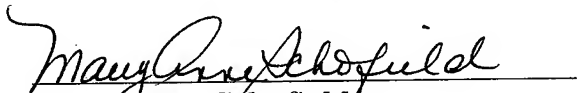

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